LETTERS TO THE EDITOR

Venoarterial connections in visceral heterotaxy

To the Editor:

We read with great interest the report of Rubino and his colleagues[1] concerning various connections in hearts from patients with visceral heterotaxy and asplenia. We[2] have just reported a similar series of findings in hearts from patients with isomeric right atrial appendages, a group of patients that is very similar but not identical to those having visceral heterotaxy and asplenia.[3] Like Rubino and his associates,[1] we have also long been interested in this spectrum of malformations, and we were surprised that the Boston investigators chose to ignore all our previous work,[4-7] because some of our findings are surely pertinent to the topic of discussion. In fact, our latest study, comprising 124 cases, produces findings that are in close agreement with the study of Rubino and associates.[1]

We disagree with the Boston group, however, on two areas of major surgical significance. The first concerns the matter of recognition of atrial arrangement (situs). Rubino and his colleagues[1] chose to ignore this matter in this publication, arguing that it had been the subject of two previous reports.[8, 9] It is, perhaps, unfortunate that neither of those earlier accounts had been the subject of peer review in the generally accepted sense, and neither is published in journal format. Be that as it may, the subject of atrial arrangement is surely the key to the concept of visceral heterotaxy, the more so since one of the cited works of Rubino's group (their reference 10)[10] contends that isomerism of the atrial chambers is an erroneous concept. This, of course, depends entirely on the concept used to differentiate the atria. For many years, we have chosen to follow the excellent concept promulgated by Van Praagh and colleagues[11] for use in recognizing and differentiating components of the cardiac segments and dubbed by them the "morphologic method." In essence, this method suggests that features that are themselves variable should preferably not be used in differentiation. It seems to us that use of this criterion rules out the venous connections as a marker of atrial morphology since, as shown by both the Rubino study[1] and our own investigation,[2] they are remarkably variable in the setting of visceral heterotaxy. Yet, if we understand the previous publications[8, 9] correctly, this is precisely the criterion they used to judge atrial "situs." Is this not a direct contravention of the morphologic method? If there were not a suitable alternative approach, such a departure would be acceptable. But an excellent alternative does exist. This is the structure of the atrial appendages based on the morphology of their junctions with the rest of the atrial segment. This emphasis on morphology is crucial, since we[2] agree with Rubino and associates[1] that neither size nor shape of the appendages is sufficiently constant to permit their recognition. Taking the extent of the pectinate muscles within the appendage relative to the vestibules of the atrioventricular junctions, in contrast, proved an absolute guide to distinction of morphologically right and left appendages not only in the normal heart, as illustrated by Van Praagh and Vlad,[12] but also in hearts from patients with visceral heterotaxy.[2] Use of this anatomic criterion enabled us in all cases studied[2] to recognize the presence of isomeric atrial appendages, not only morphologically right but also morphologically left. Venoatrial connections, however, were markedly variable, emphasizing that, in the strictest sense, it is the appendages that are isomeric and not the entire atrial chambers. This criterion of junctional morphology has also been shown to be valid in animal models of isomerism.[13, 14]

The concept of isomerism existing as a grouping within the spectrum of visceral heterotaxy then brings us to our second potential disagreement with the Boston investigators, again a feature of surgical impact. They described two cases having asplenia but in the presence of a coronary sinus. In none of our cases with isomeric right appendages (125 in all) did we encounter a coronary sinus defined on the basis of a circumflex venous channel running within the epicardial aspect of the atrioventricular junction. Indeed, the finding of anomalous coronary venous drainage is another key surgical feature in hearts with isomeric atrial appendages.[15] We wonder, therefore, if the patients in the Boston series with asplenia could have had either isomeric left appendages or, alternatively, one right and one left appendage, according to the nature of their junctions with the remainder of the atrial segment. We encountered two cases in our series with asplenia and visceral heterotaxy in which both the appendages were of morphologically left pattern.

There is then a third disagreement between our studies. Our findings showed that, according to anatomic criteria, the majority of cases in which the pulmonary veins connected to the atrial segment in hearts with asplenia and visceral heterotaxy could not be considered to represent normal connections. This is because the presence bilaterally of pectinate muscles extending around the atrioventricular junctions, together with the anomalous coronary venous drainage and the lack of atrial musculature at the insertions of the pulmonary veins, produces an arrangement quite dissimilar from the anticipated union of the pulmonary veins with the posterior wall of the morphologically left atrium. These differences have no relationship whatsoever with considerations of the site and formation of the primary and so-called secondary components of the atrial septum. At any event, as can be shown by dissecting any normal heart, the so-called secondary septum is no more than an infolding of the wall between the superior caval and pulmonary veins. The very absence of this structure, therefore, would indicate an abnormality in the arrangement of the pulmonary veins.

Robert H. Anderson, MD
Hideki Uemura, MD
William A. Devine, BSc
Department of Pediatrics
National Heart and Lung Institute
London SW3 6LY, United Kingdom

REFERENCES

1. Rubino M, Van Praagh S, Kadoba K, Pessotto R, Van Praagh R. Systemic and pulmonary venous connections in visceral heterotaxy with asplenia: diagnostic and surgical considerations based on seventy-two autopsied cases. J Thorac Cardiovasc Surg 1995;110:641-50.
2. Uemura H, Ho SY, Devine WA, Kilpatrick LL, Anderson RH. Atrial appendages and venoatrial connections in hearts from patients with visceral heterotaxy. Ann Thorac Surg 1995;60:561-9.
3. Uemura H, Ho SY, Devine WA, Anderson RH. Analysis of visceral heterotaxy according to splenic status, appendage morphology, or both. Am J Cardiol 1996;76:846-9.
4. Macartney FJ, Zuberbuhler JR, Anderson RH. Morphological considerations pertaining to recognition of atrial isomerism: consequences for sequential chamber localisation. Br Heart J 1980;44:657-67.
5. De Tommasi SM, Daliento L, Ho SY, Macartney FJ, Anderson RH. Analysis of atrioventricular junction, ventricular mass and ventriculoarterial junction in 43 specimens with atrial isomerism. Br Heart J 1981;45:236-47.
6. Sapire DW, Ho SY, Anderson RH, Rigby ML. Diagnosis and significance of atrial isomerism. Am J Cardiol 1986;58:342-6.
7. Sharma S, Devine W, Anderson RH, Zuberbuhler JR. The determination of atrial arrangement by examination of appendage morphology in 1842 heart specimens. Br Heart J 1988;60:227-31.
8. Van Praagh S, Santini F, Sanders SP. Cardiac malposition with special emphasis on visceral heterotaxy (asplenia and polysplenia syndromes). In: Fyler DC, ed. Nadas' pediatric cardiology. Philadelphia: Hanley & Belfus, 1992:589-608.
9. Van Praagh S, Kreutzer J, Alday L, Van Praagh R. Systemic and pulmonary venous connections in visceral heterotaxy with emphasis on the diagnosis of the atrial situs: a study of 109 postmortem cases. In: Clark EB, Takao A, eds. Developmental cardiology morphogenesis and function. New York: Futura, 1990:671-727.
10. Van Praagh R, Van Praagh S. Atrial isomerism in the heterotaxy syndromes with asplenia, or polysplenia, or normally formed spleen: an erroneous concept. Am J Cardiol 1990;66:1504-6.
11. Van Praagh R, David I, Wright GB, Van Praagh S. Large RV plus small LV is not single LV. Circulation 1980;61:1057-8.
12. Van Praagh R, Vlad P. Dextrocardia, mesocardia, and levocardia: the segmental approach to diagnosis in congenital heart disease. In: Heart disease in infancy and childhood. 3rd ed. Keith JD, Rowe RD, Vlad P, eds. New York: Macmillan, 1978:638-697.
13. Seo JW, Brown NA, Ho SY, Anderson RH. Abnormal laterality and congenital cardiac anomalies: relations of visceral and cardiac morphologies in the iv/iv mouse. Circulation 1992;86:642-50.
14. Morishima M, Miyagawa-Tomita S, Yasui H, Ando M, Nakazawa M, Takao A. Visceroatrial heterotaxy syndrome induced by maternal hyperthermia in the rat. Cardiol Young 1995;5:251-6.
15. Uemura H, Ho SY, Anderson RH, et al. The surgical anatomy of coronary venous return in hearts with isomeric atrial appendages. J Thorac Cardiovasc Surg 1995;110:436-44.

12/8/71008

Reply to the Editor:

Anderson, Uemura, and Devine begin by saying that we ignored all of their previous work on this subject. The purpose of our paper[1] was not to review the literature, but to present detailed morphologic anatomic data concerning the systemic and pulmonary venous connections in patients who have heterotaxy with asplenia, in order to facilitate their surgical management.

Anderson, Uemura, and Devine state that we are not following the morphologic method (that we helped to introduce)[2] because we are using the connections of the systemic and pulmonary veins to help to identify the atria. This is not true. Because the systemic veins (usually the right horn of the sinus venosus) and the pulmonary veins (the common pulmonary vein) normally are integral components of the morphologically right atrium and the morphologically left atrium,[2] respectively, these venous connections are part of the anatomic data that are used to make the diagnosis of morphologically right and left atrio. We never base the diagnosis of morphologically right or left atrium on the venous connections only. Although the pulmonary veins can be totally anomalous and may not connect at the atrial level, the systemic veins (sinus venosus) always connect with the atria. Moreover, the sinus venosus is always an integral part of the morphologically right atrium; this is not a variable.

To identify the atria morphologically, we use the following anatomic data[3, 4]: the atrial connections of the inferior vena cava and of the coronary sinus (if present); the size, shape, and location of the atrial appendages; and the atrial connections of the pulmonary veins. When all of the aforementioned morphologic data do not add up to a clear and confident diagnosis of morphologically right or left atrium, then we make the diagnosis of atrial situs ambiguus, indicating that we do not know what the atrial situs is.

Consequently, our use of the systemic and pulmonary venous connections in combination with all other available anatomic data is not a "contravention of the morphologic method," as Anderson, Uemura, and Devine allege. On the contrary, use of the venous connections in combination with all other relevant morphologic anatomic data is a good illustration of how the morphologic method is currently being used to identify the atria and the atrial situs in difficult situations that were previously regarded as undiagnosable—such as in the heterotaxy syndrome with asplenia and polysplenia.

Anderson, Uemura, and Devine say that it is unfortunate that neither of our two previous reports[3, 4] concerning the diagnosis of the atrial situs in the heterotaxy syndrome was published in a peer-reviewed journal. Some of our most important work has been published in books[2] rather than in journals. The vehicle of publication (journal or book) does not determine scientific quality.

Anderson notes that we think that "isomerism of the atrial chambers is an erroneous concept." He is right about that.[5] Anderson's own understanding of the atria in the heterotaxy syndrome has undergone remarkable changes over the past 15 years: From 1980 to 1986, it was *atrial isomerism.*[6-8] From 1988 to early 1995, it was atrial *appendage* isomerism.[9, 10] Now, Anderson, Uemura, and